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NZB mice exhibit a primary T cell defect in fetal thymic organ culture.

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Defects in T cell development have been suggested to be a factor in the development of systemic autoimmunity in NZB mice. However, the suggestion of a primary T cell defect has often been by extrapolation, and few direct observations of T cell precursors in NZB mice have been performed. Moreover, the capacity of NZB bone marrow T cell precursors to colonize the thymus and the ability of the NZB thymic microenvironment to support T lymphopoiesis have not been analyzed. To address this important issue, we employed the fetal thymic organ culture system to examine NZB T cell development. Our data demonstrated that NZB bone marrow cells were less efficient at colonizing fetal thymic lobes than those of control BALB/c or C57BL/6 mice. In addition, NZB bone marrow cells did not differentiate into mature T cells as efficiently as bone marrow cells from BALB/c or C57BL/6 mice. Further analysis revealed that this defect resulted from an intrinsic deficiency in the NZB Lin-Sca-1+c-kit+ bone marrow stem cell pool to differentiate into T cells in fetal thymic organ culture. Taken together, the data document heretofore unappreciated deficiencies in T cell development that may contribute to the development of the autoimmune phenotype in NZB mice.

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